

REMARKS

Status

This Amendment is being filed in response to the Office Action dated July 10, 2007. Claims 1, 3-17 and 19-20 were pending in the subject application. By this Amendment, Applicants have amended claims 1, 3, 4, 7, 8 and 11, and canceled claim 5, 6, 9 and 12 without prejudice, and retaining the right to represent the cancelled subject matter in a subsequent divisional or continuation application. Accordingly, claims 1, 3-4, 7, 8, 10, 11, 13-17 and 19-20, as amended, will be pending and under examination.

Applicants maintain that the amendments to the claims are fully supported by the specification as originally filed and raises no issue of new matter. Claims 1 and 3 were amended to include the subject matter of previous claims 5 and 6, specifically citalopram and escitalopram. Support for this amendment may be found in the specification as originally filed on page 20, lines 1-6. Claim 4 was amended to delete certain disease states, without prejudice, and retaining the right to represent the deleted subject matter in a subsequent divisional or continuation application. Claims 7 and 11 were amended to include the word "and" before the last species in the Markush group. Claim 8 was amended to recite the selective serotonin reuptake inhibitors citalopram and escitalopram. Support for this amendment may be found in the specification as originally filed on page 20, lines 1-6.

Accordingly, Applicant respectfully requests that the Amendment be entered.

Elections/Restrictions

On page 2 of the July 10, 2007 Office Action, the Examiner states that the arguments provided in the previous paper filed June 1, 2007 have been considered and found persuasive. Therefore the restriction requirement is withdrawn and the species election is maintained.

Applicants note that MPEP §803.02 explains that where Applicants are required to elect a species from a Markush group and "should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended."

Applicants expect that, to the extent that the election requirement is maintained, the Examiner will extend the search and examination to the full scope of the claims as required by the M.P.E.P.

Rejection of claims 1, 3 and 4 under 35 U.S.C. 112, first paragraph

On page 2 of the July 10, 2007 Office Action, the Examiner rejected claims 1, 3 and 4 under 35 U.S.C. 112, first paragraph for allegedly not enabling the person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention, commensurate in scope with these claims. The Examiner alleges that the specification does not reasonably enable all disorders as listed in claim 1 although the Examiner acknowledges that the specification is enabling for serotonin analysis and measurement of serotonin levels with citalopram and glycine transport inhibitor NFPS (specification, page 25-26). The Examiner points to the “Wands factors” for guidance (In re Wands, 8 USPq2d 140 (CAFC 1988)).

Applicants expressly **do not** concede that these are the only disease states for which the specification is enabling, however, in an effort to advance the prosecution of the subject application, but without conceding the correctness of the Examiner’s position with regard to disease states, Applicants have amended claims 1, 3 and 4 to be directed to depression, anxiety disorders and other affective disorders.

As found persuasive by the Examiner with respect to unity of invention, the Applicants have unexpectedly discovered that administering the combination of an SRI and a GlyT-1 inhibitor, in contrast to one drug alone, elevates serotonin (5-HT) levels in the ventral hippocampus of the brain. Applicants have provided adequate guidance by testing representative compounds in a common method for measuring extracellular serotonin.

With regard to the Examiner’s question of enabling disclosure with regards to disease states, Applicants maintain that effects of serotonin in the brain have been widely studied. A person of ordinary skill in the art would readily understand that an elevation in extracellular levels of serotonin in the brain would be efficacious in treating depression, anxiety disorders and other

affective disorders. The person skilled in the art can readily obtain the compounds in accordance with the claimed invention and administer the drugs for the treatment of the claimed diseases without undue experimentation. Further, to the person skilled in the art, relevant animal model systems for testing serotonin levels are routine.

Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection of Claims 1, 3 and 5 under 35 U.S.C. 112, first paragraph

On page 5 of the July 10, 2007 Office Action, the Examiner rejected claims 1, 3 and 5 under 35 U.S.C. 112, first paragraph for allegedly not enabling the person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention, commensurate in scope with these claims. The Examiner alleges that the specification does not reasonably provide enablement in a method of treating a disorder listed in claim 1 with all serotonin reuptake inhibitors and GlyT-1 inhibitors.

Applicants expressly **do not** concede that these are the only disease states for which the specification is enabling, however, in an effort to advance the prosecution of the subject application, but without conceding the correctness of the Examiner's position with regard to serotonin reuptake inhibitors and glycine transport inhibitors, Applicants have amended claims 1, 3 and 5 to recite the selective serotonin inhibitors citalopram and escitalopram. In light of the amendments to the claims and given the guidance of the specification, Applicants maintain that there is no undue experimentation needed for the person skilled in the art to make and use the invention as claimed. Applicants further maintain that the recited compounds are readily available and any experimentation by the skilled artisan would be routine.

Applicants expressly **do not** concede that these are the only serotonin reuptake inhibitors and glycine transport inhibitors for which the specification is enabling. Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection of Claims 1, 3-14 and 19 under 35 U.S.C. 103(a)

On page 8 of the July 10, 2007 Office Action, the Examiner rejected claims 1, 3-14 and 19 under 35 U.S.C. 103(a) for being allegedly unpatentable over Coppen (USP 6191133) in view of Lowe (USP 6506780) and further in view of Moltzen et al. (US 2003/0181445) and further in view of Mork et al (US 2005-0288355).

Applicants respectfully traverse the Examiner's rejection because none of the cited prior art references teach that GlyT-1 inhibitors alone or in combination with any other drug can elevate extracellular serotonin levels and thus be useful in the treatment of depression, anxiety and other affective disorders. The art teaches that glycine transport inhibitors may involve modulation of the glutaminergic and NMDA systems, by removing glycine at the NMDA synapse in the brain (see Lowe, USP 6506780, page 2, column 1 line 42 through column 2, line 2). Although the serotonin reuptake system has been widely researched and serotonin reuptake inhibitors are known to treat depression, anxiety and other affective disorders, it is unexpected that GlyT-1 inhibitors would result in augmenting the effect of an SRI (citalopram) on hippocampal serotonin levels. Only Applicants specification teaches this unexpected augmentation effect- not the prior art. Applicants respectfully direct the Examiner's attention to page 26, lines 20-27 of Applications specification in this regard.

Applicants therefore maintain that it would not be obvious to the person skilled in the art to combine selective serotonin reuptake inhibitors with glycine transport inhibitors in order to effect the serotonin system more effectively. Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection of Claims 13-16 and 20 under 35 U.S.C. 103(a)

On page 12 of the July 10, 2007 Office Action, the Examiner rejected claims 13-16 and 20 under 35 U.S.C. 103(a) for being allegedly unpatentable over Coppen (USP 6191133) in view of Lowe (USP 6506780) and further in view of Moltzen et al. (US 2003/0181445) and further in view of Mork et al (US 2005-0288355) and further in view of Carlson et al. (USP 6649614).

Applicants respectfully traverse the Examiner's rejection for the reasons stated hereinabove that the invention discloses an unexpected result that the combination of selective serotonin reuptake

inhibitor and glycine transport inhibitor compounds could not have been contemplated given the teachings of the prior art.

Rejection of Claim 17 under 35 U.S.C. 103(a)

On page 13 of the July 10, 2007 Office Action, the Examiner rejected claims 13-16 and 20 under 35 U.S.C. 103(a) for being allegedly unpatentable over Coppen (USP 6191133) in view of Lowe (USP 6506780) and further in view of Moltzen et al. (US 2003/0181445) and further in view of Mork et al (US 2005-0288355) and further in view of Gupta et al. (US2005/0014743) and Remington's: the Science and Practice of Pharmacy (Nineteenth ed., vol. 1, p. 806).

Applicants respectfully traverse the Examiner's rejection for the reasons stated hereinabove that the invention discloses an unexpected result that the combination of selective serotonin reuptake inhibitor and glycine transport inhibitor compounds could not have been contemplated given the prior art.

Applicants respectfully traverse the Examiner's rejection for the reasons stated hereinabove that the invention discloses an unexpected result that the combination could not have been contemplated given the prior art.

If a telephone interview would be of assistance in advancing prosecution of the above-identified application, applicants' undersigned attorney invites the Examiner to telephone the number provided below.

No additional fee, other than the fee for a three-month extension of time being concurrently filed, is deemed necessary with the filing of this Amendment. However, if any additional fee(s) is required, authorization is given to charge such fee(s) to Deposit Account No. 50-3201.

Respectfully submitted,

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